



Summary

Five study sites in Africa are systematically addressing resistance *P. falciparum* to antimalaria drugs and establishing the role of known and new markers of drug resistance. During the last 3 years investigators leading 5 collaborative research projects in Ghana, Mali, Nigeria, Uganda and Tanzania with partnerships in the US and Switzerland, focused on validating laboratory and clinical protocols for evaluating drug resistance. The 5 projects have emerged into a network for better understanding of drug resistance in malaria, contributing to the

Parameters for evaluating anti-malarial drug resistance

- Gene mutation(s)
- Elevated IC₅₀ *in vitro*
- Adequate plasma level of drug
- Inadequate clinical response

surveillance, monitoring and provision of local data to support malaria policy formulation. The network seeks to develop standardized methods to systematically address drug resistance in *P. falciparum* by establishing the role of specific gene mutations, in-vitro drug susceptibility, pharmacokinetics and clinical response in evaluating the extent and spread of drug resistance to commonly used antimalarials in Africa. The network builds on research projects supported by MIM/TDR RCS Task Force in partnership with WHO - AFRO, RBM and NIAID / NIH. Effort in this field is concentrated on the study of four markers of drug resistance (*see box*), establishment of a drug resistance database, improvement of clinical protocols used by the

scientists, improvement of electronic communication and expansion of the partner base. The activities of the network are designed to provide primary data on defined markers based on standard procedures with the objective of mapping resistance to antimalarial drug in the participating countries. It is anticipated that members of this multi-country network will form strong partnerships with the respective country malaria control programs to generate data useful in defining drug resistance and assessing the extent of drug antimalaria drug resistance in each site. This partnership will enhance research focused to country needs and stabilize the bridge between research, control and management of malaria in Africa. In the following sections a brief report describing the research profile and capabilities of each participant centre in the network is presented.

Network Implementation and Plan of Activities

• Marker of antimalaria drug resistance

Four markers of drug resistance in *P. falciparum* malaria (Gene mutation(s), Elevated IC₅₀ *in vitro*, adequate plasma level of drug, Inadequate clinical response) were defined in a workshop held in Geneva (June 1999).

• Field training

On-site training workshops were conducted in Bamako (January 2000) and Ouagadougou (March 2000) to test standard PCR protocols for molecular markers for field use, improve procedures for handling biological reagents, and explore ethical issues related to biomedical research.

• Study site inventory

An electronic survey was conducted to identify existing work conditions, installation, equipment, supplies, field sites, capabilities and needs for further support and training.

• Network facilitation and management.

A network manager assisted by a team of technical experts in Molecular Biology, Pharmacokinetics and Clinical pharmacology will facilitate collaboration of the network sites with WHO- AFRO on initiatives to monitor antimalarial drug resistance.

• Capacity building and project development

Analysis of site inventory data indicates the use of several protocols for evaluating clinical response to antimalaria drugs, molecular assays, *in vitro* susceptibility testing and data management. The network will work in collaboration with WHO- AFRO and RBM to implement a protocol for the assessment of patient response to antimalaria drugs. The need for stringent assessment of patient response and presentation of the data in a format that can be used by National malaria control programs is well recognized. Investigators are currently making contributions to a joint protocol for the research project and will meet early in 2002 to agree on the common protocols for follow up, sample collection and analysis. Workshops / group learning activities are proposed to build capacity in young investigators from the network sites and provide skills critical for successful implementation of the project. The workshops will focus on Clinical Management and Control of Malaria, *In vitro* Susceptibility Testing of *P. falciparum* to Antimalaria Drugs, Molecular markers of antimalarial drug resistance, Malaria Epidemiology and Community Assessment methods, Data Management and analysis, Protocols of determination of antimalarial drug levels in biological fluids and Databases support and high speed Internet connectivity.